12/1/03

COMPOSITION FOR CREATING VASCULAR OCCLUSIONS

This is a Reissue of 09/151,621, filed 9/11/98, now U.S. Patent No. 6,037,366, which

This application claims the benefit of U.S. Provisional Application No. 60/058,510, filed on Sep. 11, 1997.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a composition used to treat arteriovenous malformations ("AVMs") and other vascular abnormalities. The composition includes a cyanoacrylate liquid monomer and gold in a prepolymerized polymer of cyanoacrylate. The composition is placed into the body lumen via standard catheter procedures or directly percutaneously.

2. Description of the Related Art

AVMs and vascular tumors, especially those of the brain, are exceedingly difficult to treat. These growths may occur all over the body, but are especially difficult to treat when in the brain or brain stem. The composition of the invention is especially useful in treating neurological AVMs, but may also be used to treat tumors anywhere in the body.

Cyanoacrylate adhesives have been used surgically but are limited in their usefulness by cytotoxicity and heat generation. The brain is unusually sensitive to cytotoxicity and heat.

The art described in this section is not intended to constitute an admission that any patent, publication or other information referred to herein is "prior art" with respect to this invention, unless specifically designated as such. In addition, this section should not be construed to mean that a search has been made or that no other pertinent information as defined in 37 C.F.R. § 1.56(a) exists.

SUMMARY OF THE INVENTION

The invention provides a composition that may be placed in a body lumen including veins and arteries by super selective catheterization or direct puncture using standard tools of the interventional angiographer. The composition of the invention has been successfully tested in simulated models of the AVMs and tumors under fluoroscopy and in systems that closely resembles the neurological condition of the human body. Further studies have been done in the pig rete. The rete is a body of fine arteries that allows the blood to flow into the pig brain which closely resembles normal human AVMs.

The composition is a cyanoacrylate which involves mixing two separate containers of the material immediately prior to administration of the material into the AVM by catheter. The composition may contain seven ingredients which are divided into two parts prior to mixture and use. It furnishes properties that are useful for closing neurological AVMs. The product can also be used to close any growth resembling an AVM in any part of the body. Because of the sensitive nature of the tissues in the brain, the general sensitivity of the product must be controlled. In less sensitive areas, the product will work equally as well.

Part I consists of a cyanoacrylate liquid monomer containing pure phosphoric acid (250 ppm) hydroquinone (100 ppm) and P-methoxyphenol (1200 ppm). This composition is stable and unchanging we believe for over two years. The container in which Part I is stored requires cleaning and preparation before such stability can be achieved. The liquid monomer of choice for this usage is 2-hexyl cyanoacrylate.

Part II consists of pure powdered gold (5±3 microns), a small amount of prepolymerized polymer of the same cyanoacrylate and ethyl myristate. Any of the large chain fatty acid esters will work to replace ethyl myristate so long as they are liquids.

The pre-polymerized polymers of cyanoacrylate are unstable and change their structures and properties even in the solid state. The change is exponential and therefore the polymer must be used within a limited amount of time before deterioration occurs.

The polymer is prepared by addition of part 1 to a rapidly stirring weak bicarbonate-water solution. The addition must be added drop-wise to avoid unpolymerized masses from forming. The solid polymer is washed thoroughly with pure water to remove any traces of bicarbonate, then washed thoroughly with pure methanol to remove the water. Methanol dries rapidly and when the polymer is further dried at a high reduced pressure for 16–18 hours, it is considered dry. The polymer must be used in the next step within 24 hours to obtain consistent results in the final product. This mixture must be sterilized within 72 hours from the time of preparation.

Part II is sterilized with ethylene oxide gas with the stopper held in an open position. Ethylene oxide is an alkylating agent and after sterilization the prepolymerized polymer is stable. Hence, the stability and sterilization of part 2 are carried out simultaneously. The sterilized samples of Part II are capped in a clean room under sterile handling conditions.

The pre-polymerized polymer can be stabled by treatment with any of the strong alkylating agents, like ethylene oxide, ketene, etc.

This composition of matter has good cohesion as well as adequate adhesion to function well for AVMs and other similar uses within the vascular tree. The cohesion keeps the material together during the time required for it to polymerize. The adhesion makes it stick to the artery walls.

The polymerized device will cause a modest but desirable inflammatory response in the treated tissues.

A Formulation for Arteriovenous Malformations and Tumors

It is desirable to prepare a formulation for the intravascular occlusion of AVMs and Tumors that will have the following properties:

The product has a very slow rate of biodegradation.

Both liquid and solid forms should have excellent cohesion.

The delivered product should have medium adhesion

The delivered product must be radiopaque.

The solid polymer should be soft and pliable.

The delivered product must have a very low or negligible histotoxicity.

The deposited product must have no long term negative properties such as carcinogenicity, teratogenicity, systemic toxicity or other unpredictable biological and medical effects.

The products must be sterile.

The delivered product must have good flow characteristics for selective catheterization.

The product must be stable on storage for an extended period of time.

The formulation should be made from pure products and be reproducible for simple manufacturing procedures.